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Review Article

COMPARISON OF MORTALITY ASSOCIATED WITH SEPSIS IN THE BURN, TRAUMA, AND GENERAL INTENSIVE CARE UNIT PATIENT: A SYSTEMATIC REVIEW OF THE LITERATURE

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ABSTRACT The purpose of this systematic review of the literature was to determine the association of sepsis with mortality in the severely injured adult patient by means of a comparative analysis of sepsis in burn and trauma injury with other critically ill populations. The MEDLINE (PubMed), Cochrane Library, and ProQuest databases were searched. The following keywords and MeSH headings were used: "sepsis," septicemia," "septic shock," "epidemiology," "burns," "thermal injury," "trauma," "wounds and injuries," "critical care," "intensive care," "outcomes," and "mortality." Included studies were clinical studies of adult burn, trauma, and critically ill patients that reported survival data for sepsis. Thirty-eight articles were reviewed (9 burn, 11 trauma, 18 general critical care). The age of burn (<45 years) and trauma (34 49 years) groups was lower than the general critical care (57 64 years) population. Sepsis prevalence varied with trauma-injured patients experiencing fewer episodes (2.4% 16.9%) contrasted with burn patients (8% 42.5%) and critical care patients (19% 38%). Survival differed with trauma patients experiencing a lower rate of mortality associated with sepsis (7% 36.9%) compared with the burn (28% 65%) and critical care (21% 53%) groups. This study is the first to compare sepsis outcomes in three distinct patient populations: burn, trauma, and general critical care. Trauma patients tend to have relatively low sepsis-associated mortality; burn patients and the older critical care population have higher prevalence of sepsis with worse outcomes. Great variability of criteria to identify septic patients among studies compromises population comparisons.

KEYWORDS Outcome, prevalence, comparative analysis

INTRODUCTION

Septicemia (infection in the bloodstream) was the 10th leading cause of death in the 2006 Centers for Disease Control and Prevention report (1). In addition to the human cost, there is significant economic impact; Angus et al. (2) reported an estimated annual cost of over $16 billion as a result of sepsis therapy in the United States alone. Early detection and aggressive treatment provide opportunities to improve patient outcome by reducing intensive care unit (ICU) expenses while increasing survival for patients with sepsis (3, 4). Computer protocols have been shown to facilitate rapid detection and management of sepsis in the surgical ICU, resulting in improvement in patient outcomes (5).

Rapid evolution of the understanding of the biologic mechanisms underlying the human body's response to infection has occurred, but application of this new knowledge may complicate clear identification and effective treatment of sepsis in disparate patient populations. For instance, the American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM) definitions for sepsis (6) are based on the underlying presence of systemic inflammatory response syndrome (SIRS) and rely on presence of positive culture findings to confirm a diagnosis of sepsis (6). However, a negative culture result does not rule out the possibility of sepsis. In fact, in a large multinational study, Vincent et al. (7) noted that 40% of patients clinically identified as septic (n = 1,177) had blood cultures with no identifiable organism, a problem contributing to the complexity of identification (8). Further complicating the diagnosis, noninfectious inflammatory states such as traumatic injury, severe burns, or sterile pancreatitis meet the criteria for SIRS but not sepsis (6). To address this problem, the American Burn Association (ABA) convened a consensus group to determine burn-specific sepsis criteria, as these patients have chronic hypermetabolism and immunocompromise during hospitalization. However, these guidelines remain to be validated (9). The underlying systemic inflammatory response associated with trauma serves as a confounder for use of the ACCP/SCCM sepsis guidelines for these patients, yet no formal appraisal of the appropriateness of using SIRS criteria has been presented. Therefore, evaluation of sepsis outcomes is complicated by the inconsistent use of ACCP/SCCM definitions among published studies and unsuitable use of these guidelines within the burn and trauma communities.

To date, there have been no reviews describing outcomes for sepsis in other than general ICU patients (medical and surgical populations). Because of the physiologic differences in severe

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injury associated with burn or trauma, these patients are routinely excluded from large multicenter trials that strive for maximum homogeneity in the population studied. Furthermore, the burn patient has been proposed as representative of the universal model of trauma (10). Oftentimes, outcomes for burn and trauma patients are compared, yet no data exist to suggest whether prevalence or survival associated with sepsis is similar. The purpose of this systematic review of the literature was to determine the association of sepsis with outcomes by means of a comparative analysis of patients with sepsis in burn and trauma injury with a general critically ill population. Outcomes were mortality during ICU stay, during hospital stay, or at 28 days after hospital admission. As a secondary purpose, when reported, the prevalence of sepsis was also compared.

METHODS

A systematic review of the literature (11) was conducted using the MEDLINE (PubMed), Cochrane Library, and ProQuest (Dissertations and Theses) scientific databases. The following keywords and MeSH headings were used: "sepsis," septicemia," "septic shock," "epidemiology," "burns," "thermal injury," "trauma," "wounds and injuries," "critical care," "intensive care," "outcomes," and "mortality." Additional articles were identified from reference lists during full text review.

Studies were considered for inclusion based on review of abstracts that reported clinical studies (retrospective or prospective design) published in the English language, for primarily adult populations (>18 years of age), with information on survival of sepsis in a critically ill population. Significant changes in clinical practice in the treatment of sepsis have occurred since the first international consensus conference on sepsis (12); thus, the date range searched was limited to 1990 to 2010. Articles were excluded from review if the primary outcome measure was limited to infection, bacteremia, organ failure, or any other outcome not directly related to sepsis (infectious processes coupled with organ failure). Perinatal, non critically ill, emergency depart ment, and oncology populations were also excluded. To improve generaliz ability of ICU populations included in the analysis, further exclusion criteria eliminated single center studies, or a secondary analysis of the same pop ulation in a published study; studies of general ICU populations (primarily medical, surgical, or combination) with fewer than 1,000 patients enrolled were excluded to promote equity among number of studies included in each group. This step was deemed necessary because of the large number of sepsis reports in the literature and difficulty aggregating the overwhelming number of available studies to serve as a comparison group.

Sepsis related definitions used in this analysis include (*a*) septicemia or bacteremia: positive infection in the bloodstream; (*b*) sepsis: two or more of the criteria for SIRS, plus positive culture or clinical suspicion of infection; (*c*) severe/complicated sepsis: sepsis criteria and presence of at least one failed organ system; and (*d*) septic shock: severe sepsis in the presence of hemody namic failure unresponsive to fluid therapy, and requiring vasopressor sup port (6). The ACCP/SIRS criteria for sepsis include presence of infection with at least two of the following: temperature greater than 38°C or less than 36°C; heart rate greater than 90 beats/min; respiratory rate greater than 20 breaths/min or arterial carbon dioxide tension less than 32 mmHg; or white blood cell count less than 4,000 or greater than 12,000 cells/μL (6).

Adult populations selected for this study include (*a*) burn: thermal or chemical injury in civilian or military patients; (*b*) trauma: mechanical injury, including blunt, penetrating, or motor vehicle accident in civilian or military patients; and (*c*) general ICU: patients requiring medical or surgical intensive care management (such as mechanical ventilator support or cardiovascular support) and not primarily composed of burn or trauma injured patients. The primary outcome of interest for this review was mortality, variously defined as death during ICU stay, during hospital stay, or within 28 days after hospital admission. Prevalence of sepsis was reported when this information was available for descriptive rather than analytical purposes.

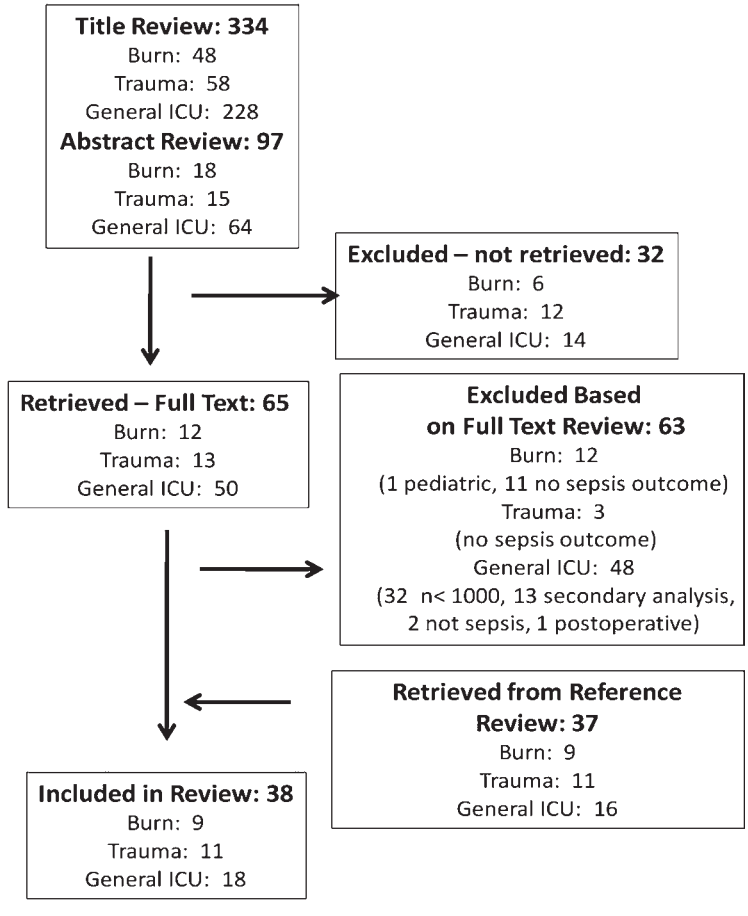

FIG. 1. **Results of search strategy.**

Methodological quality

For inclusion, studies needed an evidence rating of level II (evidence obtained from at least one well designed randomized controlled trial) to level IV (evidence from well designed, case control or cohort studies) (13). The quality of included studies was required to be either "high" (A grade) or "good" (B grade) (14). The studies that were considered "good" did not pro vide specific criteria for sepsis diagnosis. Risk of bias, such as selective out come reporting or outcome concealment, was considered during quality assessment, and no systematic bias was noted.

RESULTS

A total of 38 articles that met inclusion criteria were reviewed (burn = 9, trauma = 11, general ICU = 18) (Fig. 1). Of the nine burn studies, two studies consisted of patients included in previously reported analyses (15, 16), so these subjects were counted a single time in the total number of burn patients reported. All studies had an evidence rating of levels II through IV; quality of included studies was judged "good" or higher.

Burn studies

The nine studies reporting sepsis outcomes for the burn population, representing the time period from 1991 to 2005, include three prospective observational studies and six retrospective record reviews (Table 1). The majority were conducted at a single center (n = 7), and one study is a summary report from the ABA that represents data from 70 burn centers in 30 US states (20). A total of 2,106 burn patients with the diagnosis of sepsis of a pool of 134,159 burn admissions comprise this review. The reported mean or median age for all studies was less than 45 years, with male being the predominant sex (56%–75%) in all but one report (22). Burned patients with sepsis represent a relatively severely injured population with 30% to 76% total body surface area (TBSA) burn. Reported sepsis prevalence ranged from 8% (15) of the burn population to greater than 42% in four studies (42%–50%) (16, 18, 21, 23), and two studies reported prevalence of 50% and 65% (22, 23).

The criteria for the diagnosis of sepsis varied greatly among the studies, with two referring to the ACCP/SCCM sepsis definitions (24), three that relied on clinical criteria in addition to a positive culture result, two with culture results alone, and one with clinical criteria alone. Only two reports described the primary site of infection associated with sepsis of blood (19) and wound (21) for bacterial and fungal causes, respectively. Primary organisms associated with sepsis were identified as gram-negative in three studies (65%–72%) (19, 22, 23), gram-positive in two studies (61%–62%) (15, 17), and fungal from a single study (21).

Mortality associated with sepsis varied with degree of illness reported. The study that differentiated between uncomplicated sepsis and septic shock reported mortality rates of 6% to 11% to 27% to 63%, respectively (16). The ABA National Burn Repository 10-year review (n = 3,488) reported pulmonary failure/sepsis as the primary cause of death for 11.3%, multiple organ failure for 27.5%, and burn wound sepsis for 4% of patients (20). Variables associated with increased mortality from sepsis in the burn population were identified as multiple organ failure (15–17, 20), TBSA burn (15), and presence of inhalation injury (15, 16). The overall mortality in the National Burn Repository burned population without sepsis is reported as decreasing from 6.2% in 1995 to 4.7% in 2005 (20). Mortality for nonseptic patients was 12% compared with 33% for septic patients ($P = 0.06$) in a single-center study led by Cumming et al. (18).

Trauma studies

Trauma studies with reported outcomes of patients with sepsis (n = 11) covered the time period from 1990 to 2009, with two prospective observational studies and nine retrospective reviews (Table 2). The mechanism of injury varied, with seven that included victims of polytrauma; three included motor vehicle accidents or blunt or mechanical injury; and one comprised combat injuries. Most studies reported results from multiple centers or regional databases (n = 6) compared with reports from a single center (n = 5).

The population for this analysis includes 3,719 septic patients from a pool of more than 70,000 trauma patients. Unsurprisingly, relatively young males predominate; frequency of male sex ranged from 68% to 100% with mean age range of 34 to 49 years. The injury severity scores (ISSs) ranged from 19.3 to 47. One study reported the ISS for deaths associated with sepsis versus deaths without sepsis as 28 ± 14 vs. 13 ± 12 ($P < 0.001$), respectively (30). However, another study reported no difference between ISS for the combination of sepsis and trauma compared with trauma alone (29 ± 10 vs. 32 ± 13, not statistically significant) (34). Sources of infection or infecting organisms were not provided in any of the included studies. The definition of sepsis, when noted (n = 7), varied among reports with the ACCP/SCCM definitions (24) used in five studies (30–32, 34, 35) and *International Classification of Diseases, Ninth Revision* (*ICD-9*) codes coupled with death certificate information used in two studies (26, 29).

Mortality associated with trauma complicated by sepsis ranged from less than 7% in four studies (25, 28, 29, 33) to 10% to 23% in six other studies (26, 27, 30, 31, 35), with one study reporting 46% mortality among combat-related trauma patients with sepsis (34). One study found the difference between death from trauma alone to be significant from trauma coupled with sepsis (7.6% vs. 23%, $P < 0.001$) (30). Another team also found mortality to differ between trauma patients without sepsis and those with sepsis (9.3% vs. 36.9%, $P = 0.01$) (31). Wafaisade et al. (35) reported no significant decrease in mortality associated with sepsis in the German trauma population from 1993 to 2008, with reported mortality during consecutive 4-year periods of 16.2%, 21.5%, 22%, and 18.2%, respectively (n = 28,829; $P = 0.054$). During the same period, the authors report a decrease in the prevalence of sepsis of 14.8%, 12.5%, 9.4%, and 9.7%, respectively ($P < 0.0001$) (35). These findings suggest a reduction in the absolute mortality associated with sepsis, with an increase in the proportion of sepsis-related deaths over time in the German trauma population.

General critical care studies

Studies of critically ill patients with sepsis (n = 18) covered the time period from 1979 to 2008 and included nine prospective randomized trials or observational studies and nine retrospective studies (Table 3). One country was represented in 10 studies, with eight studies including up to 37 different

TABLE 1. **Burn studies included in analysis (n = 9)**

Burn studies	Study period	Design/evidence level (13)/quality grade (14)	Center/location	Purpose	Subjects	Sepsis subjects
Bang et al. 1998 (17)	1992 1996	Retro review/level IV/grade A	Single center; Kuwait	Retrospective review of septicemic burn patients (data included in Bang 2004)	943 admits, 280 (30%) ICU admits, 79/280 (28.2%) septic	79/280 (28.2%) ICU patients; 118 episodes
Bang et al. 2004 (15)	1992 2001	Retro review/level IV/grade A	Single center; Kuwait	Study demographic/ clinical factors associated with burn sepsis in Kuwait	2,082 hospital admits, 166 (8%) sepsis	166/2,082 (8%); 253 episodes
Cumming et al. (18) 2001 (data included in Fitzwater 2003)	1998 1999	Prosp obs/level IV/grade A	Single center; Parkland (Dallas, Tex)	Quantify complications of organ dysfunction and sepsis after burn injury	85 ICU admits (>20% TBSA); SS or septic shock = 12 (14%)	Uncomplicated sepsis 43/85 (50.6%); severe sepsis 12/85 (14.1%)
D'Avignon et al. (19) 2010	1991 2003	Retro review/level IV/grade A	Single center; USAISR (San Antonio, Tex)	Retrospective review of autopsy reports to determine incidence of death attributable to bacterial or viral cause	97 ICU patient autopsies, 27 = bacterial sepsis, 5 = viral sepsis	NR
Fitzwater et al. (16) 2003	1998 2000	Prosp obs/level IV/grade A	Single center; Parkland (Dallas, Tex)	Define relationships between sepsis, MOD, and death after burn trauma	n = 175 ICU admits (>20% TBSA, >16 y) ; sepsis: 79 (45%); complicated sepsis 30 (17%)	All sepsis = 79/175 (45%); uncomplicated sepsis 49/175 (28%), 49/79 (62%); severe sepsis 14/175 (8%), 14/79 (18%); septic shock 16/175 (9%), 16/79 (20%)
Miller et al. (20) 2006	1995 2005	Retro review/level IV/grade B	70 Center, 30 US states	Ten year review of national burn data repository	126,642 burn hospital admits (peds/adults); 18,964 with complications; 6,797/126,642 deaths (5.6%)	Septicemia complication 1,554/18,964; 1.2% of all patient cases (1,554/126,642)
Murray et al. (21) 2008	1991 2003	Retro review/level IV/grade A	Single center; USAISR (San Antonio, Tex)	Twelve year review of fungal infection and related mortality in burn autopsy	3,751 ICU admits, 228 (6.1%) deaths, 97 autopsies	43/97 (44%) fungal elements identified
Sharma et al. (22) 2006	2000 2004	Retro review/ level IV/grade A	Single center; India	Five year review of autopsy cases to determine rate of infection/sepsis in burn patients	334 autopsy cases; 216/334 (65%) ''septicemia due to burns''	NR
Sjoberg et al. (23) 2003	1997 1999	Prosp obs/level IV/grade A	2 centers; Zimbabwe	Evaluation of predicting septicemia in burn patients by using wound surface, tissue culture techniques, and blood cultures	50 ICU subjects; sepsis 21/50 (42%)	21/50 (42%) sepsis; 16/21 (76%) positive tissue CX

BP indicates blood pressure; CX, culture; gm−, Gram negative; gm+, gram positive; HR, heart rate; INH, inhalation injury; IQR, interquartile range; LOC, level of consciousness; MOD, multiple organ dysfunction; NR, not reported; Obs, observational; peds, pediatric; prosp, prospective; retro, retrospective; temp, temperature; USAISR, US Army Institute of Surgical Research.

countries; between 12 and 847 centers participated in the included reports. The populations studied comprised hospitalized or ICU patients who subsequently developed sepsis as an inpatient (7 studies) and patients admitted to the ICU with diagnosis of sepsis, severe sepsis, or septic shock (two, eight, and one study, respectively). Ultimately, more than 31.6 million septic patients were included in the studies used for this analysis among 2.08 billion studied. Various estimates of prevalence of sepsis in general medical and surgical ICU populations reviewed in this analysis were reported, ranging from 8% (38) or 1.6% to 3.2% (41, 42) of hospital admissions, up to 12% to 21% (45, 46) or 19% to 37.4% (7, 48) of ICU admissions. The mean age of patients ranged from 57 to 64 years; three studies reported that 60% to 82% of patients with sepsis

Demographics	Sepsis mortality	Sepsis definition	Site	Organism
Age mean (range) 26 y (45 d 75 y); male 56%; TBSA 46% (10 90); INH 14/79 (18%)	29% (23/79) TBSA 72% (38% 90%)	Positive blood CX based on clinical suspicion	NR	118 episodes: 62% gm+, 25% gm−, 13% mixed
Age mean (range) 26 y, 5 ± 1.4 (1 70); 60% male; TBSA 42% (2 95); INH 39/166 (23.5%), 26/39 (67%) INH died of sepsis	23.5% (39/166); mean age 31; MOF cause death 71.8%	Positive blood CX based on clinical suspicion	NR	61.3% gm+; 12% gm−; 12.7% mixed
Uncomplicated sepsis 43/85 (50.6%); severe sepsis 12/85 (14.1%)	(n = 85) Age median (IQR) 35 (24 48); male 75.3%; TBSA median 30 (23 40); INH 1/15 (7%)	Severe sepsis: 4/12 (33.3%); no sepsis: 9/73 (12.3%), $P = 0.06$	ACCP/SCCM	NR
n = 27: Age median (range) 45 (2 95); male 74%; TBSA 43% (2 81); INH bacteremic 33%, nonbacteremic 24% ($P = 0.38$)	27/97 (27.8%)	Autopsy concur with clinical status; positive blood culture; pneumonia; histological tissue invasion	Blood, pulmonary, wound	70.4% gm− (*Pseudomonas aeruginosa* 50%); 18.5 gm+; 11.1 mixed
Sepsis: age median 38 (IQR 26 49); male 86%; TBSA median 37% (IQR 29 52). IHN 22%: sepsis 11/49 (22%), severe sepsis 3/14 (21%), septic shock 7/16 (44%)	Sepsis 3/49 (6%); severe sepsis 2/14 (14%); septic shock 10/16 (63%)	ACCP/SCCM; severe sepsis: MOD score≥3; sepsis shock: pressor or acidosis	NR	NR
Age mean 33 y; male 70%; TBSA% >20 = 17%; INH 6.5%: lived 5%, died 30.7%	MOF 27.5% (958/3,488); pulmonary fail/sepsis 11.3% (395/3,488); burn wound sepsis 4.1% (142/3,488)	NR	NR	NR
Fungus attributable mortality = 14/97, age median (range) 42 (24 67), male 73%, TBSA 76% (8 92)	Mortality attributable to fungal infection 14/43 (33%), 14/97 (14.4%)	Fungal elements present in autopsy report and cause of death by pathologist	Wound, pulmonary, abdominal	*Aspergillus* 13/14 cases with fatal fungal infection (92.8%); wound primary source of infection
Age 21 25 = 30%; male 32%; TBSA mean 51% (range, <30 to >80)	216/334 (65%)	Splenic blood culture for patients with premorbid cultures	NR	65% gm−, 11% mixed
Septic: age median(range) 23 (12 56), TBSA median 30% (12 70): survived 22 (12 30) died 40 (30 70); male NR	8/16 (50%) positive tissue culture died	Temp, BP, HR, LOC	NR	72% gm−; 23% gm+ (wound tissue)

were older than 65 years (42, 51, 52), and two reported 40% to 46% of septic patients were older than 75 years (42, 52). One study reported a significant age difference between septic and nonseptic patients of 61 years versus 54 years ($P < 0.001$) (38), respectively. However, another study reported no significant difference between groups (septic 65 years vs. nonseptic 64 years, $P > 0.05$) (7). Males comprised between 47% and 64% of the patients in this analysis.

The definitions for sepsis varied among reports, with the majority using the ACCP/SCCM definitions (24) (n = 9) (2, 7, 37, 40–42, 45, 47, 48) and the remainder using *ICD-9* codes or medical record diagnoses and presence of infection with organ dysfunction [n = 5 (7, 38, 43, 49, 51) and n= 5 (36, 39, 44, 46, 50), respectively]. The primary source of infection was identified as the lung or respiratory system in all 15 studies where source was reported. The second most common source of

TABLE 2. **Trauma studies included in analysis (n = 11)**

Trauma studies	Study period	Design/evidence level (13)/quality grade (14)	Location (no. centers)	Purpose	Primary population
Esposito et al. (25) 1995	1990 1991	Retro review/level IV/grade B	Montana (NR)	Determine rate of preventable mortality and inappropriate care from traumatic death in a rural state	Mechanical trauma
Hodgson et al. (26) 2000	1991 1997	Retro review/level IV/grade B	Ontario (1)	Determine missed injuries in blunt trauma and accuracy of recorded cause of death	Blunt trauma
Maio et al. (27) 1996	1994	Pros Observ/level IV/grade B	Michigan (NR)	Determine preventable death rate, inappropriate care in rural state	Trauma
Marson and Thomson (28) 2001	1995 1997	Retro review/level IV/grade B	Brazil (NR)	Impact of pre hospital care system on MVA mortality, autopsy evaluation	MVA trauma
Meislin et al. (29) 1997	1991 1993	Retro review/level IV/grade B	Arizona (NR)	Examine traumatic death in a US county	Blunt/penetrating trauma
Osborne et al. (30) 2004	1996 1997	Retro review/level IV/grade A	Pennsylvania (28)	Characterize epidemiology of sepsis in trauma	Blunt/penetrating trauma
Plurad et al. (31) 2010	2000 2009	Retro review/level IV/grade A	CA (1)	Association between race and incidence and survival posttraumatic sepsis	Trauma
Probst et al. (32) 2009	1973 1990	Retro review/level IV/grade A	Germany (1)	Long term mortality and cause of death after multiple injuries	Polytrauma
Stewart et al. (33) 2003	1995 2001	Retro review/level IV/grade B	TX (1)	Identify preventable causes of traumatic death	Trauma
Surbatovic et al. (34) 2007	1999	Retro review/level IV/grade A	Serbia (1)	Evaluate prognostic value of immune response in combat casualties	Trauma; combat
Wafaisade et al. (35) 2011	1993 2008	Retro review/level IV/grade A	Germany (149); Central Europe (17)	Assess change in incidence, outcome, risk factors of sepsis in trauma	Trauma

hosp indicates hospital; mech, mechanical; micro, microbiology; MODS, multiple organ dysfunction syndrome; MVA, motor vehicle accident; NR, not reported; ns, non significant; observ, observational; pros, prospective; retro, retrospective; SIRS, systemic inflammatory response syndrome.

infection resulting in sepsis was the abdomen or gastrointestinal system (n = 8) (36–40, 45, 46, 50), the genitourinary tract (n = 3) (43, 44, 47), and blood (n = 3) (2, 7, 48). Of the 12 studies in which a primary infecting organism was identified, nine reported gram-positive bacteria as predominant (25%–56%) (7, 36, 40, 43, 45, 46, 48–50) compared with two reports of gram-negative bacteria (41%–49%) as cause of sepsis (37, 39). Of note, 9 studies showed no identified organism associated with clinical diagnosis of sepsis within a range of 15% to 50% of the time (36, 38–40, 43, 45, 46, 49, 53).

Mortality associated with sepsis during ICU stay was reported as ranging from 26.5% to 61% (38, 39, 45), with four studies reporting 28-day mortality of 17% to 33% (36, 40, 45, 50). The two randomized controlled trials testing drotrecogin alfa (activated) (DrotAA) therapy for septic shock that reported 28-day mortality for both intervention and control groups reached different conclusions. The majority of studies (n = 16) provided hospital mortality outcomes for patients with sepsis and severe sepsis that ranged from 18.5% to 53.6% (2, 7, 37, 39, 41–49, 51) and up to 87% for sepsis associated with failure of more than five organ systems (41).

Further analysis by Annane et al. (38) described the difference in septic shock mortality compared with nonseptic shock patients of 61.2% vs. 13.2%, respectively, for the general ICU population; matched septic shock patients with controls (n = 5,473 per group) revealed mortality of 53.8% vs. 28.2% ($P < 0.001$), respectively. In another study led by Alberti et al. (37), mortality was reported as 17% for noninfected patients compared with 53% of patients who presented to the ICU with ongoing infection. Number of involved organ systems has been associated with increased mortality; one failed system versus two is associated with increased mortality from 11% to 49% ($P = 0.001$) (46). Over time, mortality associated with sepsis has declined from 45% in 1993 to 38% in 2003 in one

Sepsis subjects	Demographics	ISS	Sepsis mortality	Sepsis definition
Mechanical trauma: 324/629 (52% of trauma related deaths)	Age mean (range) 42 (2 95), age median 36; male 74%	37 (range, 1 75) n = 227	2% (5/324)	NR
108 trauma deaths	Age median (range) 39 (2 90); male 72%	NR	17% (18/108)	Death certificate/autopsy report; SIRS criteria
65 hospital admits (25/65 died in hospital 38%)	Age mean 37.4 ± 25; male 71.6%	46.8 (range, 5 75)	10% (2/20) preventable; 3% (2/65) hospitalized	NR
243 hospital deaths (preintervention n = 128, postintervention n = 115	Age mean 34 preintervention, 35 postintervention; male 81.3% preintervention, 82.8% postintervention	NR	Preintervention 3.1% (4/128), postintervention 5.2% (6/115); overall 4.1% (10/243)	NR
340 hospitalized	Age mean 49.3; male 67.9%	25.6	Survive <60 min = 3%; 4 24 h = 5.9% 7.6%; >3 wk = 7.1%	*ICD 9* code, death certificate, autopsy report
30,303 hospitalized; 2% sepsis (606/30,303)	Sepsis: age mean 48.8 ± 21; male NR; primary source: pulmonary	Sepsis: 28.1 ± 14; no sepsis: 12.9 ± 11 ($P < 0.001$)	23% (nonseptic 7.6%, $P < 0.001$)	SIRS and infection (ACCP/SCCM)
3,998 ICU admits; 16.9% (677/3,998)	Age mean 36.7 ± 19; male 79%; Hispanic 62.4%	19.3 ± 12.7	Septic: 36.9% (250/677); nonseptic: 9.3% (310/3,321) ($P = 0.01$); total: 14% (560/3,998)	SIRS (ACCP/SCCM) and infectious source
408 (in hospital deaths); 103 (postdischarge deaths)	Age mean 29.4 ± 15.8; male 73%	Hosp deaths 29.2 ± 10.2	In hospital: 11% sepsis (45/408)	SIRS and "clinically manifest infection" (ACCP/SCCM)
753 hospital deaths	Age mean 42.5 ± 25.4, age median 39; male NR	41 ± 20.6	Combined with MODS/other 3% (23/753)	NR
76 ICU admits: sepsis = 56; nonsepsis = 20	Age mean (range) 26.8 (11 72); male 100%	Sepsis/trauma mean 29 ± 10.4; trauma 31.7 ± 12.5 (P = ns)	Nonsurvivors (n = 36), sepsis/trauma 32/56 (56%), trauma 4/20 (20%)	SIRS and positive blood culture (ACCP/SCCM)
3,042/28,829 admits; septic total = 10.2%; 1993 1996 = 14.8%, 1997 2000 = 12.5%, 2001 2004 = 9.4%, 2005 2008 = 9.7% ($P < 0.0001$)	Age mean 44 ± 19; male 81%	33 ± 13	1993 1996 = 16.2%, 1997 2000 = 21.5%, 2001 2004 = 22%, 2005 8 = 18.2 ($P = 0.054$); overall septic 19.5% vs. nonseptic 12.5% ($P < 0.0001$)	SIRS (ACCP/SCCM), no micro data in registry

report (42) and decreased during the period of 1979 to 1984 from 28% to only 18% in 1995 to 2005 in another study, despite an increase in the overall incidence of sepsis (49).

DISCUSSION

Sepsis is associated with poor outcomes in all patient populations. This review is the first to compare sepsis outcomes in three distinct patient populations: burn, trauma, and general medical/surgical critical care patients. Studies identified through a systematic review of the literature represent the available reports describing mortality associated with sepsis for these specific groups of patients, over the past two decades.

An international population is represented in this review; the majority of burn studies originate from a single center in contrast to the fact that most trauma and all general critical care studies were conducted in multiple centers. The critical care studies are especially representative of a worldwide population in which multiple countries were included in many of the reports and thus provide a homogenous comparison for this analysis. Most of the included studies are predominately chart reviews or retrospective in nature, 25 (66%) of 38, which is a limitation to the completeness of reported data.

The age of included patients appears to be different when the burn (<45 years) and trauma (34–49 years) groups are contrasted with the older general ICU population (57–64 years). Association of increased age with worse outcomes for patients with sepsis would seem to favor better outcomes for the burn population (relatively younger group in this review) when in fact the mortality rate among burn patients was more similar to the older general ICU population than to the younger trauma patients. Perhaps the effect of age is overcome by the degree of burn injury, presence of inhalation injury, and multiple organ failure (16). The ratio of males to females is greater in the burn

TABLE 3. **General critical care studies included in analysis (n = 18)**

General ICU studies	Study period	Design/evidence level (13)/quality grade (14)	Countries/centers	Purpose	Subjects
Abraham et al. (36) 2005 ADDRESS	2002 2004	PRCT/level II/grade A	34/516	APC for sepsis w/low risk of death	Severe sepsis 2,613
Alberti et al. (37) 2002	1997 1998	Cohort observ/level IV/grade A	8/28	Incidence of infection and ICU outcome	Sepsis 3,239/14,364 (22.5%) ICU admits; 1,115/3,239 (34%) septic; 944/3,239 (29%) severe sepsis; 1,180/3,239 (36%) septic shock)
Angus et al. (2) 2001	1995	Cohort observ/level IV/grade A	7 US states/847	Incidence, cost, outcome of severe sepsis in US	Septic 192,980/6,621,559 (3%) hospital admits
Annane et al. (38) 2003	1993 2000	Retro review/level IV/grade A	France/22	Update epidemiology of septic shock	100,554 ICU admits; rate 8.2% (8,251/100,554); 1993: 7%; 2000: 9.7%
Beale et al. (39) 2009	2002 2005	Cohort observ/level IV/grade A	37/276	International sepsis registry	Severe sepsis 12,570 (2 burn)
Bernard et al. (40) 2001 PROWESS	1998 2000	PRCT/level II/grade A	11/164	APC phase 3 trial for mortality reduction for severe sepsis	Severe sepsis 1,690
Dombrovskiy et al. (41) 2005	1995 2002	Retro review/level IV/grade A	US (New Jersey)/NR (data included in 2007 report)	Trend severe sepsis hospitalization, mortality, fatality rate, and impact age, race, sex	Hospital admit 7,364,550; sepsis: 233,432 (3.2%); severe sepsis: 87,675 (1.19%)
Dombrovskiy et al. (42) 2007	1993 2003	Retro review/level IV/grade A	US/NR	Trend severe sepsis hospitalization, mortality, case fatality rate	Hospital admits 391,571,824; sepsis 8,403,766 (2.15%); severe sep 2,857,476 (<1%)
Esper et al. (43) 2006	1979 2003	Retro review/level IV/grade A	US/NR	Factors that may influence health care disparities on incidence of sepsis	Hosp 930 million; sepsis 12,505,082 (1.3%)
Ferrer et al. (44) 2008	2005 2006	Before/after prosp/level IV/grade A	Spain/59 ICU	Determine if education program on SSC improves care and sepsis mortality	Sepsis: 2,319; septic shock 1,842/2,319 (79.4%) (pre: 854; post: 1,465)
Finfer et al. (45) 2004	1999 (3 mo)	Prosp observ /level IV/grade A	Australia, NZ/21 (23 ICU)	Document incidence and outcome of severe sepsis in Australia and New Zealand	691/3,543 ICU admits; 11.8% (95% CI 10.9 12.6)
Guidet et al. (46) 2005	1997 2001	Retro review/level IV/grade A	France/12 (35 ICU)	Study incidence and severity of organ dysfunction associated with sepsis	ICU admits 96,193; severe sepsis = 20, 963/96,193 (21.4%); >24 h ICU = 18, 273/65,910 (27.7%)
Levy et al. (47) 2010	2005 2008	Observ/PI project/level III/grade A	Europe, North America, South America/165	Determine compliance with severe sepsis bundles and mortality	Septic 15,022 (52% ED, 13%ICU, 35% ward
Martin et al. (48) 2009	2003 2004	Prosp observ /level IV/grade A	Canada/11 ICU	Determine acquisition, timing, and outcomes of sepsis	ICU admits 6,298; severe sepsis 1,198/6,298 (19%)
Martin et al. (49) 2003	1979 2000	Retro review/level IV/grade A	US/NR	Determine independent effect of age on sepsis	750 million hospital admits; severe sepsis 10,319,418 (1.4%)
Vincent et al. (50) 2005 ENHANCE	2001 2003	Prosp observ level III/grade A	25/361	Open label trial of APC treatment for severe sepsis	ICU sepsis 2,375 (84% had ≥2 OD)
Vincent et al. (7) 2006 SOAP	2002	Prosp observ/level IV/grade A	24/19 ICU	Define incidence of sepsis and characteristics of patients in European ICUs	ICU admits 3,174; sepsis 1,177 (37.4%); severe sepsis = 930 (30%); sep shock = 462 (15%)
Weycker et al. (51) 2003	1991 2000	Retro review/level IV/grade A	US/NR	Estimate mortality and medical charges among severe sepsis patients	Severe sepsis 16,019

Abd indicates abdominal; abx, antibiotics; APC, activated protein C; Am, America; a/w, associated with; CI, confidence interval; GI, gastrointestinal; gm−, gram negative; gm+, gram positive; GU, genitourinary; hosp, hospital; intervene, interventional; mech, mechanical; MODS, multiple organ dysfunction syndrome; MVA, motor vehicle accident; no., number; NR, not reported; ns, nonsignificant; observ, observational; OD, organ dysfunction; PRCT, prospective randomized controlled trial; pros, prospective; resp, respiratory; retro, retrospective; SIRS, systemic inflammatory response syndrome; SSC, Surviving Sepsis Campaign; Tx, treatment; UTI, urinary tract infection.

Demographics	28 Day mortality	Hospital mortality	ICU mortality	Organism/source	Sepsis definition
Intervention: age mean 58.6 ± 17; male 58.5%. control: 58.8 ± 17; male 56.3%	Intervention: 18.5%; Control: 17%			29% gm+; 24% gm−; 11% mix; 30% none/lung, ABD, UTI	Infection and sepsis induced OD
>24 h ICU age median 64 (27 83); 61.1% male		Noninfected 16.9%; infect ICU admit 53.6%		37% gm+; 49% gm−; 10% fungus/resp, GI	ACCP/SCCM
Age mean 63.8; 49.6% male		28.60%		NR/resp, blood, GU, ABD	ACCP/SCCM
Sepsis: age mean 61.4 ± 16.6; nonsepsis 53.9 ± 19, ($P < 0.001$); male septic 63.3%, nonseptic 58%			61.2% (n = 8,251) septic shock patients, 13.2% (n = 92,293) nonsepsis shock patients	NR; severe sepsis unidentified pathogen ~20%/lung, ABD, UTI	Diagnosis in medical record
Age 60.4 ± 17.5; male 59.3%		49.60%	39.20%	32.4% gm+; 41.4% gm−; 8.7% fungus; 34% undetermined/lung, ABD, UTI, blood	Infect and OD ×1 a/w sepsis
Intervention: age 60.5 ± 17.2; male 56.1%; control: age 60.6 ± 16.5; male 58%	Intervention: 24.7% 210/850; control: 30.8% 259/840 ($P = 0.01$)			25% 26% gm+; 22% 23% gm−; 13% 15% mixed; 9% fungus; 33% negative CX/lung, ABD, UTI	ACCP/SCCM: infection and SIRS and OD ×1
Severe sepsis age >60 y 75.3%, >75 y 46.5%; male 49.1%		38% with 1 OD; 87% with 5 6 OD		NR/NR	ACCP/SCCM, sepsis and OD, *ICD 9* codes
Severe sepsis age >65 y 60%; >75 y 40%; male 50.7%		1993: 45%; 2003: 37.7%		NR/NR	ACCP/SCCM, sepsis with OD, *ICD 9* codes
Age 60.5 y (95% CI 60.4 60.7): males NR		20.3% (CI 19.9 20.6)		49% 56% gm+; microbe doc infection 52%/resp, GU, GI	*ICD 9* codes infection/sepsis
Pre: age 67.4 ± 16; male 61.9%; post: 62.1 ± 16; male 60.2%		Pre: 44%; Post: 39.7%, $P = 0.04$ (overall 41.2%)		NR/resp, GU, UTI	Specific sepsis criteria, shock, and OD
Age median 60.7 ± 17.2; male 57%	32.4% (224/691)	37.5% (259/691)	26.5% (183/691)	48% gm+; 38.5% gm−; 13.2% other; CX+ 57.8% episodes/pulm, ABD, blood, skin UTI	Severe sepsis = infection, SIRS (ACCP/SCCM), OD: PROWESS
0 OD: age 55.7 ± 19, male 57%; 1 OD: age 58.2 ± 18, male 63.1%; 2 OD: age 62.1 ± 16, male 64.2%, $P < 0.001$		0 OD = 14.5%; 1 OD = 11.3%; 2 OD = 49%, $P < 0.001$		28% 42% gm+; 22.7 33.5% gm−; 2% 4% fungus; no doc infect SS1 50%, SS2 40%/pulm, ABD, CV	Infect with OD ×1 and 2
NR		Intervention 30.80%; control: 37%		NR/lung, UTI, ABD	Suspected infection, ≥2 SIRS, ≥1 OD (ACCP/SCCM)
Age 61.2 ± 16.5; male 58.8%		38.1% (CI 35.4 40.8)		35.9% gm+; 27.8% gm−; 6.4% yeast; 14% other; 15% missing/lung, blood, UTI	ACCP/SCCM and PROWESS
1979 1984: age 57.4 ± 29, male 49.6%; 1995 2000: age 60.8 ± 14, male 48%		1979 1984 = 27.8%; 1995 2000 = 17.9%		52.1% gm+; 37.6% gm−; 4.6% fungus; specific organism 51%/NR	Medical record diagnosis codes, *ICD 9*
Age 59.1 ± 17; male 58.2%	25.3% (early 22.9%, >24 h 27.4%)			26.6% gm+; 43.4% gm−; 3.7% fungi/lung, ABD, UTI	Infection, 3 of 4 SIRS, ≥1 OD
Sepsis: age 65 (range, 51 74), male 63%; Nonseptic: age 64 (49 74), male 61%		All patients = 24% (747); septic = 36% (413); nonseptic = 17% (334) ($P < 0.05$)		40% gm+; 38% gm−; 17% fungi; 18% mixed: clinical signs only 40%/resp, blood, ABD, UTI	Infect, abx, ACCP/SCCM; severe sepsis ≥1 OD
Age >65 y 81.2%; male 53.4%		21.2% ± 0.3%		NR/NR	*ICD 9* codes, infect, OD

and trauma groups compared with the general ICU patients where the ratio is more evenly matched. It is well understood that trauma and burn injuries occur in a relatively younger segment of the population and that older patients with comorbidities are more susceptible to complications of infection (54). Males tend to experience injury more frequently, but sex differences in sepsis have not been demonstrated (55, 56). Therefore, the results of this analysis reflecting age and sex differences are expected, yet conclusions must be framed with the understanding that different physiologic processes are represented in each group.

Lack of consistency in defining sepsis remains a significant hindrance to comparing clinical studies. Difficulty in accurate diagnosis due to physiologic variability among patient populations, lack of a criterion standard diagnostic test, and use of disparate criteria for treatment all conspire to make synthesis of multiple research findings problematic. Such variability is reflected in the different definitions for sepsis used in the studies included in this review (Table 4). The ACCP/SCCM international consensus definitions (24) were utilized in more than half of the general ICU studies (10/18); reliance on presence of infection coupled with various degrees of organ dysfunction or medical record diagnoses using *ICD-9* codes were used in the remainder. Wilhelms et al. (57) urge caution when *ICD-9* coding is utilized for identification of septic patients; use of three different *ICD-9* abstraction strategies resulted in generation of different patient subpopulations. The authors suggest coupling *ICD-9* codes with ACCP/SCCM sepsis criteria to improve search strategies. The ACCP/SCCM consensus definitions were used in five (30–32, 34, 35) of the seven trauma studies that reported sepsis criteria. Furthermore, use of SIRS criteria as the foundation of the ACCP/SCCM definition makes utility of these guidelines inappropriate for severely burned or trauma patients, yet two burn studies and six trauma studies relied on this method of defining sepsis. Additional complexity is added in the identification of infecting organisms because of the inconsistency of culture specimen processing coupled with a traditionally high false-negative rate (58, 59). Supporting this conclusion of problems associated with clearly defining sepsis is the discovery among the general ICU studies of nine reports with a range of 20% to 49% of patients with clinically suspected sepsis yet negative culture results (36, 38–40, 43, 45, 46, 49, 53). No method of defining sepsis has been validated in any critically ill population.

The prevalence of sepsis varied among the populations with trauma-injured patients experiencing a lower prevalence of sepsis (approximately 2.4%–16.9%) contrasted with burn (8%–42.5%) and critically ill ICU patients (19%–38%). In this analysis, it would appear that burn patients are more similar in sepsis prevalence to the general ICU population compared with trauma patients. All studies included relatively ill patients with severe burn injury between 30% and 76% TBSA burn, high trauma ISSs ranging from 19 to 47, and general ICU patients with complicated sepsis or septic shock in 9 of 18 studies. This study has not discriminated among patients admitted to the ICU for suspected sepsis from those who develop sepsis during the ICU stay; survival outcomes could in fact differ among these groups.

The source of infection associated with sepsis was not reported in any trauma studies, and only two burn studies reported primary culture source as blood and wound for bacterial and fungal organisms, respectively (19, 21). Of the 15 general ICU studies reporting the source of infection, all identified the pulmonary system as the primary origin of sepsis. The major secondary systems involved were abdominal or gastrointestinal (8/15), genitourinary (4/15), and hematologic (3/15). Unfortunately, because of lack of additional information, it is not possible to adequately compare these groups with regard to principal origin for infection in sepsis, only to surmise that the respiratory system is clearly the leading source for sepsis in the general ICU patient. The organisms associated with infection in the burn patient appeared to favor gram-negative bacteria (3/5) as predominant compared with gram-positive bacteria (2/5). Conversely, gram-positive bacteria were identified as the principal cause of septic infection in the general ICU population (10/15) versus gram-negative bacteria (2/15). With no data reported for trauma studies reviewed and minimal burn study data, it can safely be concluded that for the general ICU population the most frequent septic infections occur secondary to gram-positive bacteria. There appears to be a tendency for gram-negative organisms to predominate in the severely burned population, resulting in implications for empiric antibiotic coverage in different patient groups (60).

Survival outcomes were different among populations with civilian trauma patients experiencing a relatively lower rate of mortality associated with sepsis (7%–23%) when compared with the burn (28%–65%) and general ICU (21%–53%) groups (Fig. 2). Mortality-related sepsis for the combat trauma patients (34) of 46% appears to be more similar to the burn and general ICU patients, perhaps because of evacuation delays or varying injury pattern. This report of combat trauma casualties may not represent the civilian trauma population and in this review is considered an outlier. Interesting results from a large 20-year German study (n = 29,829) demonstrate a reduction in the incidence of sepsis over the two decades but with no reduction in sepsis-associated mortality (35). Such findings underscore the difficulty treating sepsis in the severely injured patient. Organ

TABLE 4. **Sepsis definition used in each study**

	Not reported	ACCP/SCCM SIRS	*ICD 9*/diagnosis	Autopsy	Clinical presentation	Organ failure/dysfunction	Positive culture/infection
Burn n 9	1	2		3	5	1	2
Trauma n 11	4	6	1	2			4
General ICU n 18		10	7		6	4	10

Most studies used more than one method for identifying septic patients.

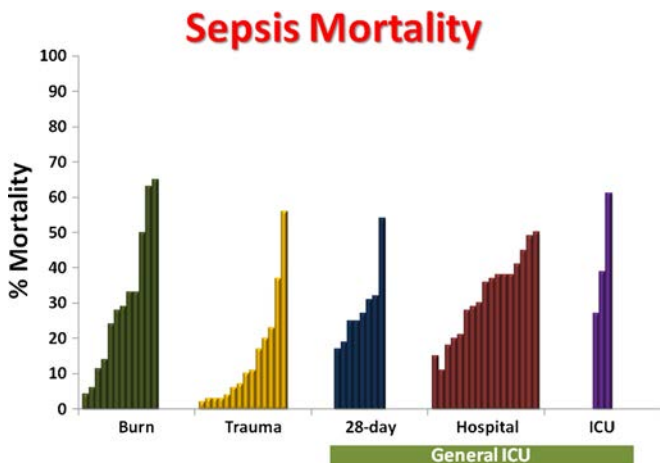

FIG. 2. **Mortality rates associated with sepsis**. Each bar represents reported mortality from each included study. Some studies reported several rates; all rates are included.

dysfunction was found to be associated with greater mortality in burn and general ICU patients. In addition, the absence of sepsis was found to confer a significant reduction in mortality in a burn (18) and septic ICU population (38) (12% and 13% nonseptic vs. 33% and 61% septic, respectively). Thus, prevention of infection when possible, early aggressive treatment when infection is identified, and attenuation of organ failure may provide means to reduce death in patients with sepsis.

Dramatic improvements in the systematic and aggressive treatment of sepsis have resulted from application of early goal-directed therapy (61), large international consensus conferences (62), and powerful pharmacological agents such as DrotAA (40). However, the problem of accurate and relevant diagnostic criteria remains, despite diligent attempts at developing agreement (12, 24). Complicating the diagnosis of sepsis in the trauma and burn populations, underlying systemic inflammatory processes make the standard ACCP/SCCM sepsis criteria useless in the burn population and questionable for use in trauma; furthermore, the ABA consensus-based sepsis criteria require validation (9). Perhaps criteria based on the PIRO approach, incorporating predisposition, infection, response, and organ dysfunction, will improve identification of the septic patient (63).

Published meta-analyses reporting outcomes of large populations of general critical care patients substantiate the poor outcomes associated with sepsis noted in this review. Although DrotAA has not been shown to significantly improve survival in low-risk patients when compared with placebo (36, 64, 65), the reported mortality for a cohort of 4,329 patients with APACHE II score of greater than 25 was 30.6% for treated patients versus 38.3% for placebo ($P = 0.007$) (65). Aggressive fluid resuscitation strategies have been shown to reduce mortality for early intervention versus late intervention from 39% to 64%, respectively, in a meta-analysis of 1,001 subjects (66). Administration of intravenous immunoglobulin therapy as a treatment for sepsis was associated with lower mortality, 25.8% in treated patients compared with 30.3% in placebo-treated patients (risk ratio, 0.74; 95% confidence interval, 0.62–0.89; n = 2,621) (67). Finally, routine use of corticosteroids has been reported to confer no survival benefit in septic patients, with 35.3% (388/1,099) 28-day mortality rate in the treatment group compared with 38.5% (400/1,039) in the control group ($P = 0.05$) of meta-analysis of randomized studies (68). Thus, the available meta-analyses and systematic reviews further support the observation of high risk of death associated with sepsis in the critically ill patient.

Review limitations

Limitations of this review include the inability to perform a statistical analysis because of lack of standardized reporting and heterogeneity among studies (69) and availability of few studies in the burn and trauma populations that report sepsis-related outcomes in sufficient detail for comparison. Restriction of included general critical care studies was necessary to facilitate synthesis as hundreds of quality research studies have been published that discuss sepsis-related outcomes. The majority of included trauma studies are dated; thus, this comparison may not reflect current outcome patterns. Definitions used for sepsis vary greatly among studies, and no definitions have been validated for any ICU population. Many ICU patients are admitted because of sepsis, whereas burn and trauma patients develop sepsis during hospitalization; the time effect of sepsis onset on the findings of this study is unknown. Despite these limitations, significant patterns have emerged from this review supporting the premise that sepsis outcomes differ among the burn, trauma, and general ICU populations.

Future directions for knowledge development

Advances in the understanding of the complex pathophysiology of the syndrome of sepsis are occurring rapidly and will ultimately lead to more accurate diagnostic tools, better criteria for diagnosis, and significantly reduced mortality. Improved outcomes over time have been demonstrated despite an increased prevalence of sepsis (42, 49); thus, with advancements in technology and improved mechanistic understanding of the syndrome, this trend toward improved survival is expected to continue. Initiatives such as the Surviving Sepsis Campaign (47, 62) have already demonstrated improved outcomes associated with early and aggressive treatment of sepsis. A barrier remains in accurate and early detection of uncomplicated sepsis, so progressive organ dysfunction may be averted, and survival maximized. Biomarkers such as procalcitonin, C-reactive protein, and lactate show promise in facilitating diagnosis, especially when coupled with other clinical signs and symptoms (70, 71). Validation of clinical criteria for unique patient populations is essential for clearly defining sepsis in all studies (3). The advent of computer decision support technology at the bedside provides the opportunity to combine multiple predictors in real time and aid the clinician in the detection of early sepsis (5, 72–75).

SUMMARY

Sepsis is a common and oftentimes fatal diagnosis that varies among critically ill populations. Trauma patients tend to have a relatively low incidence and associated mortality with sepsis, yet severely burned patients and the older general ICU population have higher prevalence and worse outcomes. Although severe burn injury represents an extreme model of traumatic injury, with regard to sepsis these populations differ significantly. The

younger burn patient appears to more closely resemble the general critically ill ICU patient considering susceptibility and survivability of sepsis, although the primary infecting organism and source of infection differ. Systemic inflammatory response syndrome–based definitions for sepsis that are applicable to the general ICU population are inappropriate for use in the burn and trauma populations. Validated sepsis criteria are necessary for all unique patient populations. The lack of consistent use and inappropriate application of sepsis criteria among studies make comparison problematic. Much has been done to develop consensus-based aggressive treatment protocols, yet early detection of sepsis remains elusive because of the lack of definitive criteria. Technological advances in assay development and computer decision support promise to provide the means for sepsis identification, leading to significant improvement in patient outcomes.

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